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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,095	04/12/2001	Yoshihiro Kawaoka	800.026US1	5332

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EXAMINER	
MCKELVEY, TERRY ALAN	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/834,095	KAWAOKA, YOSHIHIRO	
	Examiner	Art Unit	
	Terry A. McKelvey	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *2-4,7,8,10-24 and 27-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,9,25,26 and 32* is/are rejected.

7)☒ Claim(s) *5 and 31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/12/04 has been entered.

Election/Restrictions

Claims 1, 5-6, 9, 25-26, and 31-32 are directed to the elected invention and species, elected with traverse in the papers filed 8/7/02 and 6/16/03.

Claims 2-4, 7-8, 10-24, and 27-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention or species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirements in the papers filed 8/7/02 and 6/16/03.

Claim Objections

Claims 1, 5-6, 9, 26, and 31-32 are objected to because of the following informalities: Claim 1 recites "in the absence amantadine". This is grammatically incorrect: it should be "in the absence of amantadine". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6, 9, 25-26, and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new rejection necessitated by the applicant's amendment to the claims 2/12/04. The applicant's arguments drawn to the instant rejection were carefully considered, but they were not deemed to be persuasive.

The claims are drawn to an isolated and purified recombinant influenza virus comprising a mutant (M2) protein which lacks or has reduced activity relative to the corresponding wild-type ion channel protein, wherein the mutation is in the transmembrane domain of the ion channel protein, and wherein the mutation does not alter the in vitro replication of the virus in the absence (of) amantadine, but is associated with attenuation of the virus in vivo. These product claims are genus claims because they encompass influenza viruses having any mutation in the transmembrane domain of the M2 protein (or another ion channel protein in influenza virus), but which have the indicated functional properties. About 13 different species are specifically claimed.

However, the specification describes six mutants in the transmembrane region (all of the M2 protein, and none in a different ion channel protein), only three of which, M2A30P (a single amino acid substitution), M2del29-31 (a three amino acid deletion), and M2HATM (and a substitution of the transmembrane domain) meet the functional limitations of the claims. The other three mutants of this region, M2V27T, M2S31N, and M2W41A all lack the claimed functional limitation with regard to attenuation in vivo. The prior art of record, Sweet et al, teaches a mutation in the transmembrane domain of M2, which does

not have the functional limitation as claimed. See the withdrawn art rejection of record. The specification and claims do not indicate what distinguishing structural attributes are shared by the members of the genus which distinguish them from other mutants in the transmembrane domain that lack the functional limitations as claimed because, of the mutants in the transmembrane domain of record in the specification and the prior art, over half of them do not have the functional properties as claimed and thus there is no correlation between structure (mutations in the transmembrane domain of an ion channel protein) and function (does not substantially alter the in vitro replication of the virus in the absence of amantadine, but is associated with attenuation of the virus in vivo). The specification and claims do not place any limit on the number of amino acid substitutions, deletions, insertions, and/or additions that may be made to the M2 protein (or other ion channel protein) transmembrane region to result in mutant viruses having the claimed functional properties. Thus, the scope of the claims includes numerous structural variants of the claimed products, and the genus is highly variant because a significant number of structural differences between the genus members is permitted.

Although these types of changes are routinely done in the art, the specification and claims do not provide any description as to what changes can or should be made to result in viruses having the claimed functional properties, except for providing three specific species of only one ion channel protein, none of which have the same kind of mutation (one substitution, one deletion, and one replacement mutation is taught that meets the claim limitations). The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common structural attributes or characteristics that identify the members of the claimed genus which have the functional limitation, and because the members of the genus are highly variant, this clearly shows that there is insufficient description of the claimed genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus which has the functional limitations as claimed. Thus, applicant was not in possession of the claimed genus.

Response to Arguments

The applicant argues that Applicant has described the common structural attributes of members of the claimed genus, a

recombinant influenza virus with at least one substitution or a deletion in the transmembrane domain of the influenza virus ion channel protein, and functional characteristics coupled with a known or disclosed correlation between function and structure, the presence of the substitution or the deletion does not substantially alter the in vitro replication of the virus in the absence of amantadine but is associated with attenuation in vivo. This argument is not persuasive for the following reasons. First, the specification only teaches the species that meet the functional limitation with regard to only one ion channel protein, the M2 protein. No mutants of the NB protein of influenza B and no mutants of the CM1 protein of influenza C were taught which meet the claim limitations. Even though these are the ion channel proteins from the other influenza species, they are different from M2 and there is no description of mutants of these other ion channel proteins which provide a structure/function correlation. Second, as described in the instant rejection set forth above, although some mutants in the transmembrane domain of the M2 protein meet the functional limitations of the claimed invention, a majority of those of record do not meet the functional limitation despite meeting the structural limitation as claimed. Thus, there is no correlation between structure and function because making a mutation in the

transmembrane domain of M2 does not predictably result in the functional properties as claimed.

The applicant argues that as for the number of substitutions or size of deletions in the transmembrane domain, the nucleotide substitutions or deletion in the ion channel gene is such that the resulting recombinant virus can be isolated, that is, the virus must be viable in vitro. Thus, alterations in the transmembrane domain which do not yield viable virus are not within the scope of the claims. This argument is not persuasive in overcoming the instant rejection for the following reason. The instant rejection is not based upon whether the claimed virus can be isolated (which is an argument drawn to enablement which is not instantly questioned), but instead it is drawn to whether the application has described the claimed invention which is drawn to a genus of mutants which have particular functional limitations. The specification describes three very specific mutants which meet the claim limitations both structurally and functionally and three which meet the structural limitations, but not the functional limitations (and one is taught in prior art of record which also lacks the functional limitations.) Based upon this analysis, there is no clear correlation between structure and function. For any given mutant that meets the structural limitation, one of skill in the

art would not know whether it would meet the functional limitation. For example, does a mutation from S31 to any of 18 other amino acids not tried result in a mutant meeting the claimed functional limitation? Which ones? Does a deletion from amino acid 32 to amino acid 35 result in a claimed mutant? Thus, the application fails to describe the other members of the genus as claimed, despite limiting the mutants to having mutations in the transmembrane domain of an ion channel protein. The application is claiming mutants most of which have not been described because there is no description of what mutants in the transmembrane domain of M2 or other ion channel proteins meet the claimed functional limitations, except for the three specific mutants specifically described for M2.

Conclusion

No claims are allowed.

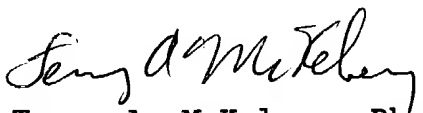
Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 703-872-9306. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO

DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning rejections or other major issues in this communication or earlier communications from the examiner should be directed to Terry A. McKelvey whose telephone number is (571) 272-0775. The examiner can normally be reached on Monday through Friday, except for Wednesdays, from about 7:30 AM to about 6:00 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to his office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached on (571) 272-0781.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Terry A. McKelvey, Ph.D.
Primary Examiner
Art Unit 1636

April 18, 2004